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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,313	05/14/2001	Terry B. Strom	01948-056001	8786

26161 7590 03/11/2003

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EXAMINER
HAMUD, FOZIA M

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/855,313	Strom et al
Examiner	**Art Unit**
Fozia Hamud	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Dec 9, 2002*.

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-42* is/are pending in the application.

4a) Of the above, claim(s) *12 and 18-41* is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1-11, 13-17, and 42* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [X] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). *7*
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

DETAILED ACTION

Election/Restriction

1. Applicants' election with traverse of the invention of Group I (claims 1-11 and 13-17), in Paper No. 15, filed on 09 December 2002 is acknowledged.

Applicants' ground of traversal is that the claims of Groups I and VIII are related, as they cover products and a processes of making those products, respectively. Accordingly, Applicants request that Groups I and VIII be examined together.

This ground of traversal is persuasive, therefore, the invention of Group I (claims 1-11 and 13-17) and the invention of Group VIII (claim 42) will be searched and examined together. Thus, claims 1-11, 13-17 and 42 are under consideration.

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 12 and 18-41 are withdrawn from consideration by the Examiner as they are drawn to non-elected inventions.

Information Disclosure

2. The reference DE 19823351 A1 cited in the information discourse statement (PTO-1449) submitted by Applicants on 25 March 2002, in Paper NO: 7 has not been considered, because it is not translated. The other references submitted on 25 March have been considered. However, none of the references cited in the information discourse statement (PTO-1449) submitted by Applicants on 11 April 2002, in Paper NO: 12 have been considered, because these references have not been matched with the case. Therefore, it is kindly requested that Applicants submit the references again for consideration in the next office action. Any inconvenience is regretted.

Claim rejections-35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-11, 13-17 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a mutant of interleukin-15 (IL-15), said mutant having mutations at positions 149 and 156 of the polypeptide of SEQ ID NO:2, wherein a glutamine is replaced with an aspartate , said composition also comprising a CTLA4/Ig polypeptide and a method of making said composition, does not reasonably provide enablement for "all" possible compositions comprising a first agent that targets an IL-15 receptor and a second agent that inhibits "all" possible costimulatory signals transmitted between a T cell and an antigen-presenting cell (APC). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Instant claims 1 and 42 are drawn to a therapeutic compositions comprising a first agent that targets an IL-15 receptor and a second agent that inhibits a costimulatory signal transmitted between a T cell and APC and a method of making said compsotion. The claims encompasses "all" possible compositions comprising "all" possible agents that target an IL-15 receptor and "all" possible agents that inhibit "all" possible costimulatory signals transmitted between a T cell and an antigen-presenting cell (APC), and method of making such, however, instant specification discloses a mutant of IL-15, said mutant having mutations at positions 149 and 156 of the polypeptide of SEQ ID NO:2,

wherein a glutamine is replaced with an aspartate and a CTLA4/Ig polypeptide, (see figures 2 and 3). The specification demonstrates that allograft survival is dramatically improved when an allograft recipient is treated with IL-15 mutant and CTLA4/Ig polypeptide, (see page 27 line 23 through page 28 line 6 and figure 3).

The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant application, it will be undue experimentation to make "all" possible compositions comprising "all" possible agents that target an IL-15 receptor and "all" possible agents that inhibit "all" possible costimulatory signals transmitted between a T cell and APC. Instant specification only discloses one IL-15 mutant with specific substitutions, and one specific agent (CTLA4/Ig) that binds to B7, blocks B7/CD28 interaction and thus inhibits T-cell activation, while instant claims 1-3, 10-11, 13-15 and 17 encompass "all" possible agents that target IL-15 receptors as a first agent or "all" possible mutants of IL-15,"all" possible agents that inhibit "all" possible costimulatory signals transmitted between a T cell and an APC. The only polypeptide that binds to B7 molecule that is enabled is the CTLA4/Ig polypeptide. With respect to claims reciting "IL-15 mutant", instant specification does not give guidance as to how to generate IL 15 mutants, other than the disclosed one. With respect to claim 10, instant specification discloses an IL-15 mutant with an Fc region that might have a

cytocidal activity, therefore, the specification is non-enabling for "all" possible moieties that "leads to the elimination of IL-15R bearing cells". Instant specification does not give any guidance as to how to generate the claimed composition. Furthermore, the state of the art is such that amino acid modifications of proteins is unpredictable, thus one of ordinary skill in the art would not be able to predict which mutations to Il-15, would result in a mutant which has the desired activity. Therefore, the quantity of experimentation to determine "all" possible "all' possible compositions comprising a first agent that targets an IL-15 receptor and a second agent that inhibits "all" possible costimulatory signals transmitted between a T cell and an APC, are practically infinite and the guidance provided in the specification very little. Absent further guidance from the specification it would constitute undue experimentation to determine all "all' possible compositions comprising "all" possible agents that target an IL-15 receptor and "all" possible agents that inhibit "all" possible costimulatory signals transmitted between a T cell and an APC, the claims are not commensurate in scope with the specification but rather are much broader than the supporting disclosure.

4b. Claims 1-11 and 13-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only discloses being enabling for a composition comprising a mutant of interleukin-15 (IL-15), said mutant having mutations at positions 149 and 156 of the polypeptide of SEQ ID NO:2, wherein a glutamine is replaced with an aspartate, said composition also comprises a CTLA4/Ig polypeptide, is not commensurate in scope with the claims

drawn to "all" possible compositions comprising a first agent that targets an IL-15 receptor and a second agent that inhibits "all" possible costimulatory signals transmitted between a T cell and an antigen-presenting cell (APC), or claims drawn to "all" possible IL-15 mutants or "al possible polypeptides bind to a B7 molecule.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Instant specification only defines the structure of the IL-15 mutant with the specific subistutions mentioned above, and does not describe the structure of any other IL-15 mutant. Applicants have not disclosed which other residues of the polypeptide of SEQ ID NO:2 can be substituted or deleted. Furthermore, the only polypeptide that binds to B7 molecule described in the instant specification is the CTLA4/Ig. With the exception the IL-15 mutant comprising mutations at positions 149 and 156 of the polypeptide of SEQ ID NO:2, wherein a glutamine is replaced with an aspartate the skilled artisan cannot envision the detailed structure of the encompassed IL-15 mutants. Also with the exception of the polypeptide CTLA4/Ig, the skilled artisan can not envision all other polypeptides that bind to B7 molecules, therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of making it.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Therefore only a composition comprising a mutant of interleukin-15 (IL-15), said mutant having mutations at positions 149 and 156 of the polypeptide of SEQ ID NO:2, wherein a glutamine is replaced with an aspartate and a CTLA4/Ig polypeptide and a method of making said composition.

Claims 4-9 and 16 are rejected under 35 U.S.C. 112, first paragraph, insofar as they depend on claim 1 for the limitations set forth directly above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claim 2 is indefinite because the claim recites ".....substantially pure mutant.....", because the degree of purity desired is not clear and is not described in the specification. Appropriate correction is required.

4b. Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the claim is drawn to a method of making the claimed composition by purifying the mutant IL-15 polypeptide and the polypeptide that binds to B7 from expression systems and combining the two, however the claim does not recite what the expression systems comprise, and how to combine the two polypeptides. Is simply mixing the two polypeptides sufficient to make the desired composition? What conditions should be used to combine the two polypeptides? Appropriate correction is required.

Conclusion

5. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Thursdays from 7:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER

Art Unit 1647
06 March 2003